Impact of Treatment With Tenofovir Alafenamide or Tenofovir Disoproxil Fumarate on Hepatocellular Carcinoma Incidence in Patients with Chronic Hepatitis B

Young-Suk Lim,1 Wai-Kay Seto,2 Queen Ning,1 Calvin Q. Pan,1 Namiki Izumi,1 Scott K. Fung,2 Namiki Izumi,1 Scott K. Fung,2 Young-Suk Lim1
1Department of Gastroenterology, Liver Center, Asian Medical Center, University of Ulsan College of Medicine; 2State Key Laboratory of Liver Research, The University of Hong Kong. Department of Infectious Diseases, Tongji Hospital Affiliated to Tongji Medical College, Huazhong University of Science and Technology; Division of Gastroenterology and Hepatology, Department of Medicine, NYU Langone Health, NYU School of Medicine, New York, NY, USA; 3Department of Gastroenterology and Hepatology, Massachusetts General Hospital, Boston, MA, USA; 4University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, CA, USA; 5Department of Infectious Diseases, Bankstown Hospital, Bankstown Medical Centre, Sydney, NSW, Australia

Background and Aim

- Tenofovir alafenamide (TAF) – Novel tenofovir (TVP) prodrug with greater plasma stability, enhanced hepatic uptake, and lower circulating TVP levels relative to tenofovir disoproxil fumarate (TDF).
- TAF has shown efficacy noninferior to TDF with improved bone and renal safety through 96 weeks in virostatic chronic B (CHB) patients, and 48 weeks in virally suppressed patients who switched from TDF to TAF.

- Antiviral therapy reduces the risk of hepatocellular carcinoma (HCC) in CHB patients.
- Recent studies suggest differences may exist in HCC risk reduction among first-line treatments for CHB.

- Study aim: Evaluate HCC incidence and impact of antiviral treatment with TAF or TDF over 5 years in two ongoing Phase 3 studies.

Methods: Hepatocellular Carcinoma Assessment

- HCC was a predefined adverse event (AE).
- Screening, diagnosis, and treatment as per local standards of care.
- Hepatic ultrasonography (every 6 mo) added at Week 96.

- Baseline predictors of HCC by MV analysis: Age (HR 1.11; p < 0.001), male gender (HR 7.57; p = 0.007).

- Early discontinuations: TAF n=3 (AE, withdrew consent, death); TDF n=4 (AE, investigator discretion, death).

- Additional follow-up and further assessment of HCC risk reduction using other risk estimators is needed to confirm these results.

Conclusions

- In >1800 HBVAg-positive and –negative patients with CHB enrolled in 2 large Phase 3 studies, antiviral treatment for 5 years demonstrated:
  - Low rates of HCC with TAF or TDF treatment (1% and 1.9%, respectively); cumulative incidence (by KM) did not differ for TAF vs TDF.
  - Lack of HCC normalization at Week 24, advanced age, male gender, and cirrhosis were predictors of HCC development by MV analysis.
  - Significant reduction in HCC incidence vs predicted rates by REACH-B was seen for all cases and cirrhosis-defined cases.
  - In patients treated with TAF, a significant reduction in SIR was seen; for TDF there was a trend.

- Additional follow-up and further assessment of HCC risk reduction using other risk estimators is needed to confirm these results.

Study Design

- Two Phase 3, randomized, DB, active-controlled trials (global and China cohorts).

- Study 108 (N=797): TAF vs安慰剂
  - Study 110 (N=1053): HBVAg-positive patients

- Key inclusion criteria: HBV DNA >2000 IU/mL, ALT ≥40 (males) or ≥30 IU/mL (females), with/without compensated cirrhosis, eGFR ≥50 mL/min; no evidence of HCC (recent imaging).

- 2.1 randomization: stratified by HBV DNA level and treatment status (n/w/experienced).

- Cumulative HCC incidence plotted by Kaplan-Meier method. Baseline and on-treatment predictors for HCC assessed by multivariable (MV) analysis using Cox proportional hazards regression model.

- Predetermined HCC incidence calculated by REACH-B risk score.

- Baseline demographics and disposition: TAF and TDF cases.

- Baseline and on-treatment predictors of HCC by MV analysis: Age (HR 1.11; p < 0.001), male gender (HR 7.57; p = 0.007).

- Early discontinuations: TAF n=3 (AE, withdrew consent, death); TDF n=4 (AE, investigator discretion, withdrew consent, noncompliance).

- HBV DNA and ALT Normalization Over 240 Weeks

- Baseline on-treatment predictors of HCC development by MV analysis.

- Conclusions

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